In the Claims

1. (three times amended) [The] A method for determining the relative ratio of [LDL to HDL or] at least two different apolipoproteins in a biological sample comprising:

immersing into the sample a solid phase material having separately immobilized thereon at least first and second monoclonal antibody molecules immunoreactive with LDL, HDL or VLDL or at least two different apolipoproteins, wherein the first and second monoclonal antibodies bind to [either] different stable, conformation independent epitopes that are uninfluenced by the lipid content of the lipoprotein, apolipoprotein or lipid associated with the specific lipoprotein, wherein the lipoproteins are selected from the group consisting of LDL, HDL [or] and VLDL [or to different apolipoproteins in a conformation and lipid content independent manner];

allowing the monoclonal antibody molecules time to bind to the LDL, HDL or VLDL or apolipoproteins in the sample;

removing the solid phase material containing the immobilized monoclonal antibody molecules;

determining the amount of LDL, HDL or VLDL lipoprotein or at least two different apolipoproteins bound by the immobilized monoclonal antibody molecules, and

comparing the amount bound which is specific for LDL, HDL or VLDL or each apolipoprotein in order to calculate the relative amounts of LDL, HDL or VLDL or apolipoproteins.

4. (twice amended) The method of claim 3, wherein the first or second monoclonal antibodies [comprise] are the anti-LDL monoclonal antibody produced by the hybridoma cell line HB_3cB_3 ATCC designation number HB 11612.

5. (twice amended) The method of claim 3, wherein the first or second monoclonal antibodies [comprise] are recombinant anti-LDL $RcB_3M_1D_4$ ATCC designation number 69602.

9. (three times amended) The method of claim 6 further comprising measuring the amount of apolipoprotein or protein associated with lipid in the sample, further comprising the step of providing [antibody] antibodies immunoreactive with the [apolipoproteins] apolipoprotein, wherein the antibodies are coupled to a protein stain, and staining the apolipoprotein or protein associated with lipid in the sample by reacting the protein stain coupled antibodies with the apolipoprotein or protein associated lipid in the sample.

12. (three times amended) A method of determining the relative concentration of at least two different apolipoproteins in a biological sample comprising:

mixing in solution a first and second monoclonal antibody molecules each immunoreactive with a specific different apolipoprotein into the sample, wherein at least one of the first and second monoclonal antibodies bind to a stable,

conformation independent epitope that is uninfluenced by the lipid content of a lipoprotein, apolipoprotein or lipid associated with a specific lipoprotein selected from the group consisting of different apolipoproteins in a conformation and lipid content independent manner;

allowing the monoclonal antibody molecules to bind to the apolipoprotein in the sample,

immersing into the mixture third immobilized monoclonal antibody molecules immunoreactive with a second, distinct epitope of one of the apolipoproteins,

allowing the third immobilized monoclonal antibody molecules to bind to one of the [apolipoprotein] apolipoproteins bound by either the first or second monoclonal antibodies,

detecting the presence of the apolipoprotein bound by [both one of] either the first [and] or second monoclonal antibodies and the third immobilized monoclonal antibodies, and

determining the amount of apolipoprotein bound by [both one of] either the first [and] or second monoclonal antibodies and the third immobilized monoclonal antibodies.

39. (twice amended) A method for determining the relative ratio of LDL to HDL in a biological sample comprising

(a) determining the amount of LDL in the sample by

adding to the sample monoclonal antibody molecules immunoreactive with low density lipoprotein and not cross-reactive with high density lipoprotein and determining the amount of low density lipoprotein;

(b) determining the amount of HDL in the sample by

adding to the sample monoclonal antibody molecules immunoreactive with high density lipoprotein and not cross-reactive with low density lipoprotein and determining the amount of high density lipoprotein; and

(c) determining the ratio of the amount of low density lipoprotein with the amount of high density lipoprotein, wherein at least one of the monoclonal antibodies to LDL and HDL bind [in a conformation and lipid content independent manner] a stable, conformation independent epitope that is uninfluenced by the lipid content of the lipoprotein, apolipoprotein or lipid associated with the specific lipoprotein.

40 (twice amended) A method for determining the relative ratio of VLDL to HDL in a biological sample comprising

(a) determining the amount of VLDL in the sample by

determining the amount of Apo C-III present in the VLDL in the sample by providing Pan B antibody which is characterized by an equal binding and high affinity for all Apo B-containing lipoproteins in human plasma,

providing monoclonal antibody specifically immunoreactive with Apo C-III,

contacting the anti-ApoC-III antibody reactive with Apo C-III with the biological sample to form complexes between the anti-ApoC-III antibody and the Apo C-III containing lipoprotein particles,

contacting the Pan B antibody with the biological sample containing the anti-ApoC-III antibody bound to the Apo C-III containing lipoprotein particles,

separating the complexed Pan B-anti-ApoC-III antibody-lipoprotein particles from the biological sample, which is the amount of Apo C-III present in VLDL in the anti-Apo C-III anti-Apo B complexed material in the sample; and

(b) determining the amount of HDL in the sample by

determining the amount of Apo C-III present in the HDL in the sample by

providing Apo A-I monoclonal antibody specifically immunoreactive with Apo A-I,

providing monoclonal antibody specifically immunoreactive with Apo C-III,

contacting the antibody reactive with Apo C-III with the biological sample to form complexes between the anti-Apo C-III antibody and the Apo C-III containing lipoprotein particles,

contacting the anti-Apo A-I antibody with the biological sample to form complexes with the anti-Apo C-III antibody-Apo C-III containing lipoprotein particles,

separating the complexed [antibody-] <u>anti-Apo C-III antibody-Apo C-III containing</u> lipoprotein particles from the biological sample,

determining the amount of Apo C-III present in HDL in the anti-Apo C-III-anti-Apo A-I complexed material in the sample, and

determining the ratio of Apo C-III present in VLDL in the sample [and] to Apo C-III present in HDL in the sample, which is the ratio of VLDL to HDL,

wherein the VLDL and HDL are measured in the same sample using immobilized anti-Apo A-I and anti-Apo B or anti-Apo C-III antibodies or measured by immunoprecipitation with the anti-Apo A-I and anti-ApoB antibodies or anti-Apo C-III antibodies in separate samples,

wherein at least one of the monoclonal antibodies bind to a stable, conformation independent epitope that is uninfluenced by the lipid content of the lipoprotein, apolipoprotein or lipid associated with a specific lipoprotein selected from the group consisting of Apo AI, Apo B, [or] and Apo CIII [in a conformation and lipid content independent manner].

41. (twice amended) A method for determining the relative ratio of VLDL to HDL comprising

(a) determining the amount of VLDL in the sample by

determining the amount of Apo E present in the VLDL in the sample by

providing Pan B antibody which is characterized by an equal binding and high affinity for all Apo B-containing lipoproteins in human plasma,

providing monoclonal antibody which specifically binds to Apo E associated with VLDL,

contacting the antibodies reactive with Apo E associated with VLDL with the biological sample to form complexes between the anti-ApoE antibodies and Apo E containing particles,

contacting Pan B antibody with the biological sample containing the complexes between the anti-ApoE antibodies and ApoE containing particles to form complexes of anti-ApoB-anti-ApoE-ApoE containing particles, and

determining the amount of Apo E in the complexes of anti-ApoB-anti-ApoE-ApoE containing particles, which is the Apo E present in VLDL in the sample;

(b) removing the complexes of anti-ApoB-anti-ApoE-ApoE containing particles, either by binding of the anti-Apo E antibodies to an immobilized surface or centrifugation of sample to remove the complexes of anti-ApoB-anti-ApoE-ApoE containing particles;

and

(c) determining the amount of HDL in the sample by

determining the amount of Apo E present in the HDL in the sample by

providing Apo A-I monoclonal antibody immunoreactive specifically with Apo A-I,

[providing monoclonal antibody which binds to Apo E associated with HDL,]

contacting the antibodies reactive with Apo E with the biological sample to form complexes between the anti-ApoE antibodies and Apo E containing particles,

contacting [Pan B] the Apo A-I monoclonal antibody with the biological sample [for] to form complexes of the anti-ApoE antibodies-ApoE containing particles-anti-[ApoB] ApoA-I,

determining the amount of Apo E present in HDL in the complexes of the anti-ApoE antibodies-ApoE containing particles-anti-[ApoB] Apo A-I in the sample, and

determining the ratio of Apo E present in VLDL in the sample and Apo E present in HDL in the sample which is the ratio of VLDL to HDL,

wherein at least one of the monoclonal antibodies bind to a stable, conformation independent epitope that is uninfluenced by the lipid content of the lipoprotein, apolipoprotein or lipid associated with a specific lipoprotein selected from the group consisting of Apo B, Apo AI, [or] and Apo E [in a conformation and lipid content independent manner].

42. (twice amended) A kit for determining the relative ratio of VLDL to HDL comprising

Pan B antibody which is characterized by an equal binding and high affinity for all Apo B-containing lipoproteins in human plasma,

monoclonal or recombinant antibody specifically immunoreactive with Apo C-III, and

monoclonal or recombinant Apo A-I antibody specifically immunoreactive with Apo A-I,

wherein at least one of the monoclonal or recombinant antibodies specifically bind to a stable, conformation independent epitope that is uninfluenced by the lipid content of the lipoprotein, apolipoprotein or lipid associated with a specific lipoprotein selected from the group consisting of Apo B, Apo AI, [or] and Apo CIII [in a conformation and lipid content independent manner].

44. (twice amended) A kit for determining the relative ratio of VLDL to HDL comprising

Pan B antibody which is characterized by an equal binding and high affinity for all Apo B-containing lipoproteins in human plasma,

monoclonal antibody which predominantly binds to Apo E associated with VLDL ,

monoclonal Apo A-I antibody specifically immunoreactive with Apo A-I, and

monoclonal antibody which predominantly binds to Apo E in HDL,

wherein at least one of the antibodies binds to a stable, conformation independent epitope that is uninfluenced by the lipid content of the lipoprotein, apolipoprotein or lipid associated with a specific lipoprotein.

45. (twice amended) The kit of claim 44 wherein the anti-Apo E or anti-Apo A-I monoclonal [or recombinant] antibody molecules are selected from the group consisting of monoclonal antibodies, recombinant antibodies, and monoclonal antibody fragments [that specifically bind to a stable, conformation independent epitope which is uninfluenced by the lipid content of the lipoprotein, apolipoprotein, or lipid associated with a specific lipoprotein].